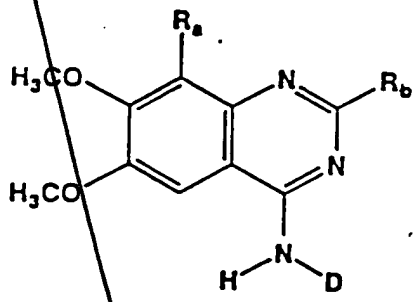
CLAIMS

What is claimed is:

1. A nitrosated or nitrosylated α-adrenergic receptor antagonist selected from the group consisting of:

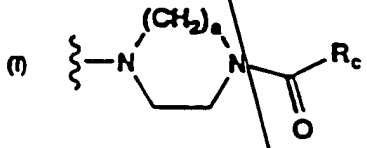
(i) a compound having structure I:

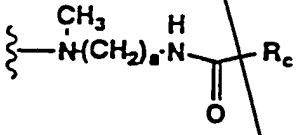


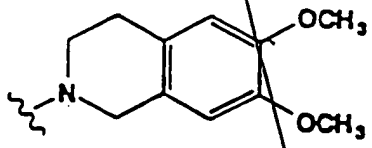
I

wherein R_a is a hydrogen or an alkoxy;

R_b is:



(ii)  or

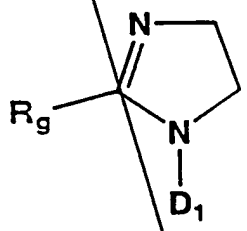
(iii) 

wherein a is an integer of 2 or 3;

R_c is a heteroaryl, a heterocyclic ring, a lower alkyl, a hydroxyalkyl, or an arylheterocyclic ring;

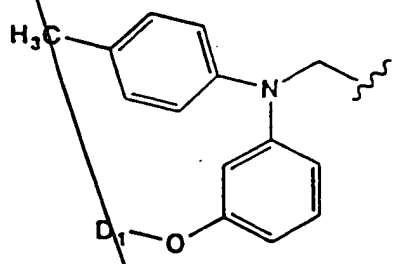
D is (i) -NO, (ii) $-NO_2$, (iii) $-C(R_d)-O-C(O)-Y-Z-(C(R_e)(R_f))_p-T-Q$, wherein R_d is a hydrogen, a lower alkyl, a cycloalkyl, an aryl, an arylalkyl, or a heteroaryl; Y is oxygen, sulfur, carbon or NR_i wherein R_i is a hydrogen or a lower alkyl; R_e and R_f are each independently a hydrogen, a lower alkyl, a haloalkyl, a cycloalkyl, an alkoxy, an aryl, a heteroaryl, an arylalkyl, an amino, an alkylamino, a dialkylamino, an amido, an alkylamido, a carboxylic acid, a carboxylic ester, a carboxamido, a carboxy or -T-Q, or R_e and R_f taken together are a carbonyl, a heterocyclic ring, a cycloalkyl or a bridged cycloalkyl; p is an integer from 1 to 10; T is independently a covalent bond, oxygen, sulfur or nitrogen; Z is a covalent bond, a lower alkyl, a haloalkyl, a cycloalkyl, an aryl, a heteroaryl, an arylalkyl, a heteroalkyl, an arylheterocyclic ring or $(C(R_e)(R_f))_p$, and Q is -NO or $-NO_2$;
(iv) $-C(O)-Y-Z-(G-(C(R_e)(R_f))_q-T-Q)_p$ wherein G is a covalent bond, -T-C(O)-, -C(O)-T- or T, wherein q is an integer from 0 to 5, and wherein R_e, R_f, p, Q, Z, Y and T are as defined above, or (v) $-P-Z-(G-(C(R_e)(R_f))_q-T-Q)_p$, wherein P is a carbonyl, a phosphoryl or a silyl, and wherein R_e, R_f, p, q, Q, T, Z and G are as defined above.

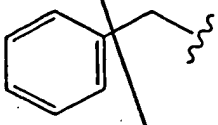
(ii) a compound having structure II:

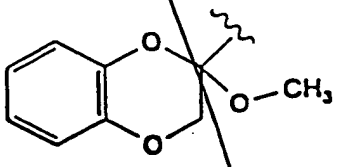


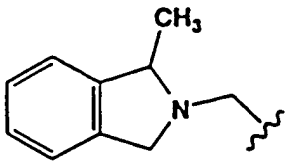
II

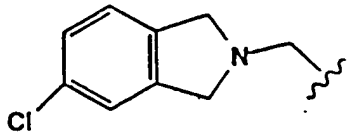
wherein, R_g is:

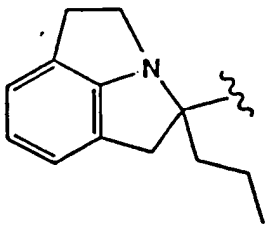
(i) 

(ii) 

(iii) 

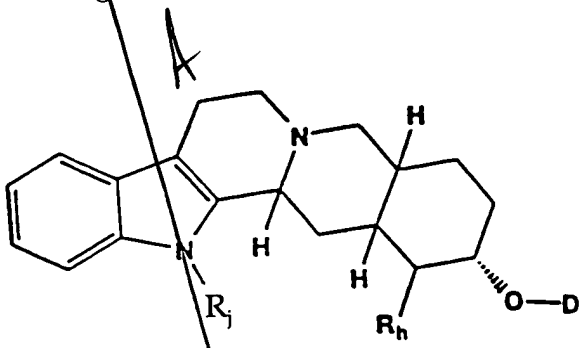
(iv) 

(v)  or

(vi) 

wherein D_1 is a hydrogen or D, wherein D is as defined above, with the proviso that D_1 must be D if there is no other D in the compound;

(iii) a compound having structure III:

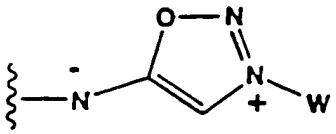


III

wherein R_h is a hydrogen, -C(O)-OR_d or -C(O)-X, wherein X is

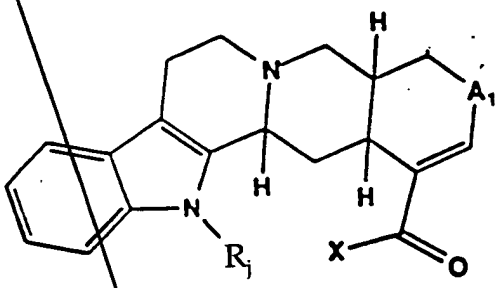
(1) -Y-$(C(R_e)(R_f))_p$-G-$(C(R_e)(R_f))_p$-T-Q, wherein G is a covalent bond, -T-C(O)-, C(O)-T-, or -C(Y-C(O)-R_m)-, wherein R_m is a heteroaryl or a heterocyclic ring; and wherein Y, R_d, R_e, R_f, p, Q and T are as defined above; or

(2)



wherein W is a heterocyclic ring or $NR_iR'_i$, wherein R_i and R'_i are independently a lower alkyl, an aryl, or an alkenyl; and wherein R_j is -D or $-(O)CR_d$, wherein D and R_d are as defined above;

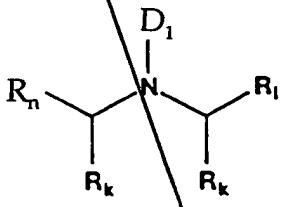
(iv) a compound having structure IV:



IV

wherein A_1 is an oxygen or a methylene, and X and R_j are as defined above;

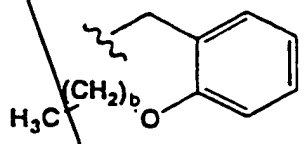
(v) a compound having structure V:

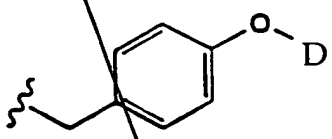


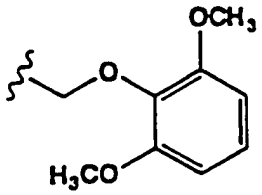
V

wherein R_k is independently a hydrogen or a lower alkyl;

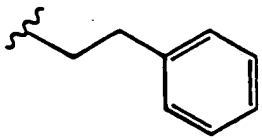
and R_l is:

(i) 

(ii) 

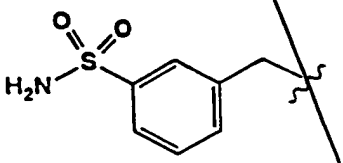
(iii) 

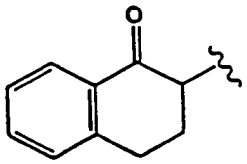
or

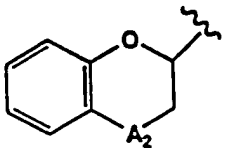
(iv) 

wherein b is an integer of 0 or 1; D_1 is as defined above; and

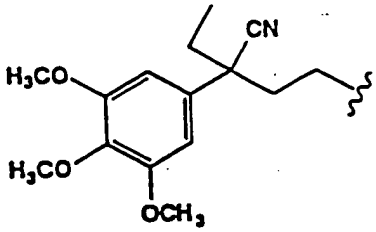
R_n is:

(i) 

(ii) 

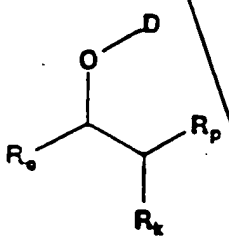
(iii) 

or

(iv) 

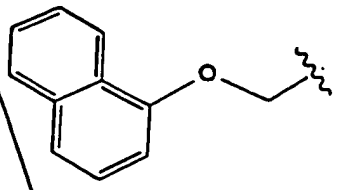
wherein A_2 is an oxygen or a sulfur:

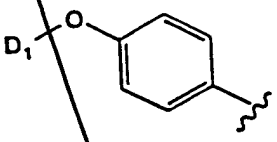
(vi) a compound having structure VI:



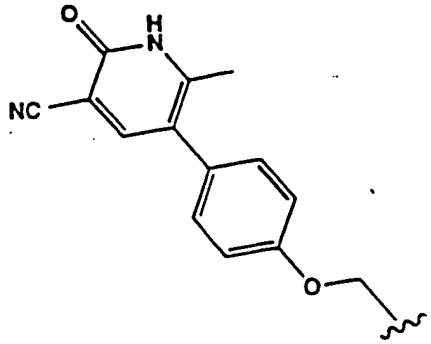
VI

wherein R_o is:

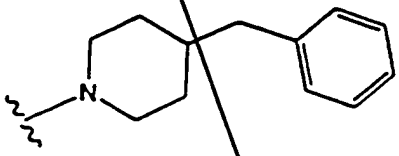
(i) 

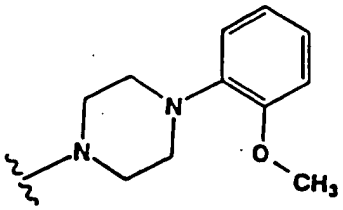
(ii) 

or

(iii) 

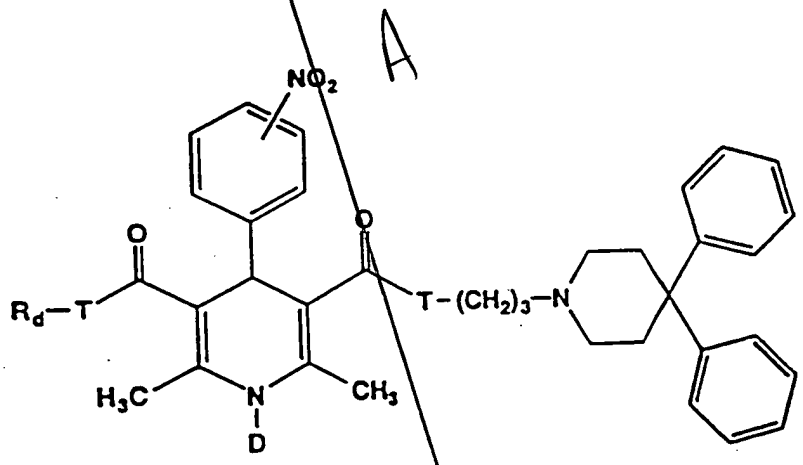
and R_p is:

(i) 

or (ii) 

and R_k, D and D_1 are as defined above; and

(vii) . a compound having structure VII:



VII

wherein R_d, T and D are defined as above.

2. The nitrosated or nitrosylated α-adrenergic receptor antagonist of claim 1, wherein the nitrosated or nitrosylated α-adrenergic receptor antagonist is a nitrosated or nitrosylated member selected from the group consisting of a haloalkylamine, an imidazoline, a quinazoline, an indole derivative, a phenoxypropanolamine, an alcohol, an alkaloid, an amine, a piperazine and a piperidine.

3. The nitrosated or nitrosylated α-adrenergic receptor antagonist of claim 2, wherein the haloalkylamine is selected from the group consisting of phenoxybenzamine and dibenamine;

wherein the imidazoline is selected from the group consisting of phentolamine, tolazoline, idazoxan, deriglidole, RX 821002, BRL 44408 and BRL 4409;

wherein the quinazoline is selected from the group consisting of prazosine, terazosin, doxazosin, alfuzosin, bunazosin, ketanserin, trimazosin and abanoquil;

wherein the indole derivative is selected from the group consisting of carvedilol and BAM 1303;

wherein the alcohol is selected from the group consisting of labetalol and ifenprodil;

wherein the alkaloid is selected from the group consisting of ergotoxine, ergocornine, ergocristing, ergocryptine, rauwolscine, corynathine, raubascine, tetrahydroalstonine, apoyohimbine, akuammignie, β-yohimbine, yohimbol, pseudoyohimbine and epi-3α-yohimbine;

wherein the amine is selected from the group consisting of tamsulosin, benoxathian, atipamezole, tedisamil, mirtazipine, setiptiline, reboxitine, delequamine, chlorpromazine, phenothiazine, BE 2254, WB 4101 and HU 723;

wherein the amide is selected from the group consisting of indoramin and SB 216469;

wherein the piperazine is selected from the group consisting of naftopil, saterinone urapidil, 5-methylurapidil, monatepil, SL 89.0591 and ARC 239; and

wherein the piperidine is haloperidol.

4. A composition comprising the nitrosated or nitrosylated α-adrenergic receptor antagonist of claim 1 and a pharmaceutically acceptable carrier.

5. A method of treating a sexual dysfunction in an individual in need thereof comprising administering to the individual the composition of claim 4 to treat the sexual dysfunction.

6. The method of claim 5, wherein the individual is female.

7. The method of claim 5, wherein the individual is male.

8. A composition comprising (i) the nitrosated or nitrosylated α-adrenergic receptor antagonist of claim 1 and (ii) a compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor.

9. The composition of claim 8, wherein the compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor is an S-nitrosothiol.

10. The composition of claim 9, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-homocysteine, S-nitroso-cysteine or S-nitroso-glutathione.

11. The composition of claim 9, wherein the S-nitrosothiol is:

(i) $CH_3(C(R_e)(R_f))_xSNO$;

(ii) $HS(C(R_e)(R_f))_xSNO$;

(iii) $ONS(C(R_e)(R_f))_xB$; or

(iv) H_2N-$(CO_2H)(CH_2)$-C(O)NH-$C(CH_2SNO)$-C(O)NH-CH_2 -CO_2H

wherein x equals 2 to 20; R_e and R_f are independently a hydrogen, a lower alkyl, a haloalkyl, an alkoxy, a carboxylic acid, a carboxylic ester, a cycloalkyl, an aryl, a hereroaryl, an arylalkyl, an alkylamino, a dialkylamino, or -T-Q, or R_e and R_f taken together are a carbonyl, a heterocyclic ring, a cycloalkyl or a bridged cycloalkyl; T is a covalent bond, oxygen, sulfur or nitrogen, Q is NO or NO_2, and B is a fluoro, an alkoxy, a cyano, a carboxamido, a cycloalkyl, an arylkoxy, an alkylsulfinyl, an arylthio, an alkylamino, a dialkylamino, a hydroxy, a carbamoyl, an N-alkylcarbamoyl, an N,N-dialkylcarbamoyl, an amino, a hydroxyl, a carboxyl, a hydrogen, a nitro or an aryl.

12. The composition of claim 8, wherein the compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor is:

(i) a compound comprising at least one ON-O-, ON-N- or ON-C- group;

(ii) a N-oxo-N-nitrosoamine comprising an R_1R_2-$N(O\text{-}M^+)$-NO group, wherein M^+ is a metal cation; and R_1 and R_2 are independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic hydrocarbon, or a heterocyclic compound;

(iii) a thionitrate having the structure R_{10}-S-NO_2, wherein R_{10} is a polypeptide, an amino acid, a sugar, an oligonucleotide, or a straight or branched, saturated or unsaturaed, aliphatic or aromatic hydrocarbon; or

(iv) a nitrate having the structure R_{10}-O-NO_2, wherein R_{10} is as defined above.

13. The composition of claim 12, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-N-polypeptide, an ON-C-polypeptide, an ON-N-amino acid, an ON-C-amino acid, an ON-N-sugar, an ON-C-sugar, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, substituted or unsubstituted, saturated or unsaturated, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, substituted or unsubstituted, saturated or unsaturated, aliphatic or aromatic ON-C-hydrocarbon, an ON-N-heterocyclic compound or an ON-C-heterocyclic compound.

14. The composition of claim 8, wherein the compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor is L-arginine or OH-arginine.

15. The composition of claim 8, wherein the compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor is a compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group.

16. The composition of claim 15, wherein the compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group is an O_2N-O-polypeptide, an O_2N-N-polypeptide, an O_2N-S-polypeptide, an O_2N-C-polypeptide, an O_2N-O-amino acid, an O_2N-N-amino acid, an O_2N-S-amino acid, an O_2N-C-amino acid, an O_2N-O-sugar, an O_2N-N-sugar, an O_2N-S-sugar, an O_2N-C-sugar, an O_2N-O-oligonucleotide, an O_2N-N-oligonucleotide, an O_2N-S-oligonucleotide, an O_2N-C-oligonucleotide, a straight or

branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-S-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-C-hydrocarbon, an O_2N-O-heterocyclic compound, an O_2N-N-heterocyclic compound, an O_2N-S-heterocyclic compound or an O_2N-C-heterocyclic compound.

17. A method of treating a sexual dysfunction in an individual in need thereof comprising administering to the individual the composition of claim 8 in a pharmaceutically acceptable carrier to treat the sexual dysfunction.

18. The method of claim 17, wherein the individual is female.

19. The method of claim 17, wherein the individual is male.

20. A composition comprising (i) an α-adrenergic receptor antagonist and (ii) a compound that donates, transfers or releases nitric oxide or elevates endogenous levels of endothelium-derived relaxing factor.

21. The composition of claim 20, wherein the α-adrenergic receptor antagonist is a haloalkylamine, an imidazoline, a quinazoline, an indole derivative, a phenoxypropanolamine, an alcohol, an alkaloid, an amine, a piperazine or a piperidine.

22. The composition of claim 21, wherein the haloalkylamine is selected from the group consisting of phenoxybenzamine and dibenamine;

wherein the imidazoline is selected from the group consisting of phentolamine, tolazoline, idazoxan, deriglidole, RX 821002, BRL 44408 and BRL 4409;

wherein the quinazoline is selected from the group consisting of prazosine, terazosin, doxazosin, alfuzosin, bunazosin, ketanserin, trimazosin and abanoquil;

wherein the indole derivative is selected from the group consisting of carvedilol and BAM 1303;

wherein the alcohol is selected from the group consisting of labetalol and ifenprodil;

wherein the alkaloid is selected from the group consisting of ergotoxine, ergocornine, ergocristing, ergocryptine, rauwolscine, corynathine, raubascine, tetrahydroalstonine, apoyohimbine, akuammignie, β-yohimbine, yohimbol, pseudoyohimbine and epi-3α-yohimbine;

wherein the amine is selected from the group consisting of tamsulosin, benoxathian, atipamezole, tedisamil, mirtazipine, setiptiline, reboxitine, delequamine, chlorpromazine, phenothiazine, BE 2254, WB 4101 and HU 723;

wherein the amide is selected from the group consisting of indoramin and SB 216469;

wherein the piperazine is selected from the group consisting of naftopil, saterinone urapidil, 5-methylurapidil, monatepil, SL 89.0591 and ARC 239; and

wherein the piperidine is haloperidol.

23. The composition of claim 20, wherein the compound that donates, transfers or releases nitric oxide is an S-nitrosothiol.

24. The composition of claim 23, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-homocysteine, S-nitroso-cysteine or S-nitroso-glutathione.

25. The composition of claim 23, wherein the S-nitrosothiol is:

(i) $CH_3(C(R_e)(R_f))_xSNO$;

(ii) $HS(C(R_e)(R_f))_xSNO$;

(iii) $ONS(C(R_e)(R_f))_xB$; or

(iv) H_2N-$(CO_2H)(CH_2)$ -C(O)NH-$C(CH_2SNO)$-C(O)NH-CH_2 -CO_2H

wherein x equals 2 to 20; R_e and R_f are independently a hydrogen, a lower alkyl, a haloalkyl, an alkoxy, a carboxylic acid, a carboxylic ester, a cycloalkyl, an aryl, a hereroaryl, an arylalkyl, an alkylamino, a dialkylamino, or -T-Q, or R_e and R_f taken together are a carbonyl, a heterocyclic ring, a cycloalkyl or a bridged cycloalkyl; T is a covalent bond, oxygen, sulfur or nitrogen, Q is NO or NO_2, and B is a fluoro, an alkoxy, a cyano, a carboxamido, a cycloalkyl, an arylkoxy, an alkylsulfinyl, an arylthio, an alkylamino, a dialkylamino, a hydroxy, a carbamoyl, an N-alkylcarbamoyl, an N,N-dialkylcarbamoyl, an amino, a hydroxyl, a carboxyl, a hydrogen, a nitro or an aryl.

26. The composition of claim 20, wherein the compound that donates, transfers or releases nitric oxide is:

(i) a compound comprising at least one ON-O-, ON-N- or ON-C- group;

(ii) a N-oxo-N-nitrosoamine comprising an R_1R_2-$N(O\text{-}M^+)$-NO group, wherein M^+ is a metal cation; and R_1 and R_2 are independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic hydrocarbon, or a heterocyclic compound;

(iii) a thionitrate having the structure R_{10}-S-NO_2, wherein R_{10} is a polypeptide, an amino acid, a sugar, an oligonucleotide, or a straight or branched, saturated or unsaturaed, aliphatic or aromatic hydrocarbon; or

(iv) a nitrate having the structure R_{10}-O-NO_2, wherein R_{10} is as defined above.

27. The composition of claim 26, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-N-polypeptide, an ON-C-polypeptide, an ON-N-amino acid, an ON-C-amino acid, an ON-N-sugar, an ON-C-sugar, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, substituted or unsubstituted, saturated or unsaturated, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, substituted or unsubstituted, saturated or unsaturated, aliphatic or aromatic ON-C-hydrocarbon, an ON-N-heterocyclic compound or an ON-C-heterocyclic compound.

28. The composition of claim 20, wherein the compound that elevates levels of endogenous endothelium-derived relaxing factor is L-arginine or OH-arginine.

29. The composition of claim 20, wherein the compound that donates, transfers or releases nitric oxide or elevates levels of endogenous endothelium-derived relaxing factor is a compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group.

30. The composition of claim 29, wherein the compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group is an O_2N-O-polypeptide, an O_2N-N-polypeptide, an O_2N-S-polypeptide, an O_2N-C-polypeptide, an O_2N-O-amino acid, an O_2N-N-amino acid, an O_2N-S-amino acid, an O_2N-C-amino acid, an O_2N-O-sugar, an

O_2N-N-sugar, an O_2N-S-sugar, an O_2N-C-sugar, an O_2N-O-oligonucleotide, an O_2N-N-oligonucleotide, an O_2N-S-oligonucleotide, an O_2N-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-S-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic O_2N-C-hydrocarbon, an O_2N-O-heterocyclic compound, an O_2N-N-heterocyclic compound, an O_2N-S-heterocyclic compound or an O_2N-C-heterocyclic compound.

31. A method of treating a sexual dysfunction in an individual in need thereof comprising administering to the individual the composition of claim 20 in a pharmaceutically acceptable carrier to treat the sexual dysfunction.

32. The method of claim 31, wherein the individual is female.

33. The method of claim 31, wherein the individual is male.

34. A compound comprising a nitrosated or nitrosylated α-adrenergic receptor antagonist.